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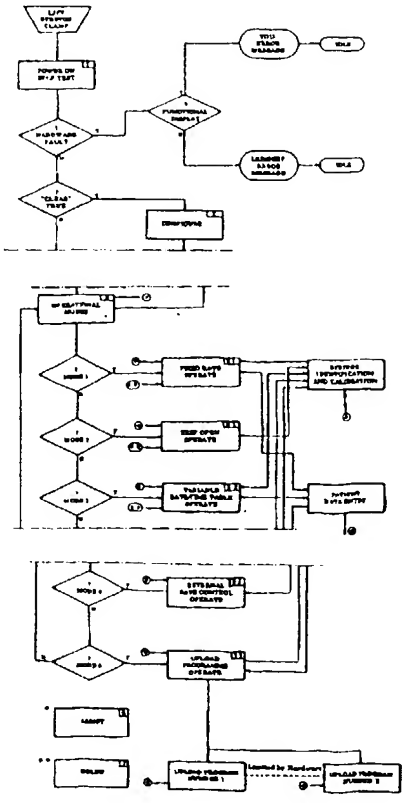
(54) Title: FIELD PROGRAMMABLE INTRAVENOUS INFUSION SYSTEM

(57) Abstract

A system for controlling the operation of an infusion pump including means for controlling the rate of infusion of a drug or other solution by the infusion pump into a patient, user programmable microprocessor means for defining a predetermined rate of infusion profile or pattern for a predetermined drug or solution, a user operable scaling means for programming the microprocessor means to control the overall size of the predetermined rate infusion profile or pattern and thereby determine the amount of drug or solution delivered to the patient, and user operable means for activating the infusion pump to cause infusion of the drug or solution according to the user programmed information.



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Field Programmable Intravenous Infusion System

Field of the Invention

This invention relates to infusion systems by means of which drugs and other solutions can be delivered intravenously or otherwise infused into a patient.

Background of the Invention

Recently, systems have been developed for the specific purpose of administering intravenous anaesthetic agents, chemotherapeutic agents and other short acting drugs. These systems usually incorporate the names of drugs and data relating to the pharmacokinetic properties of the drugs. This pre-programmed or manufacturer-programmed information is then used during operation of the system to deliver drug from the infusion system in order to achieve a level of drug either in the blood of the patient or predicted to occur at the site in the body where the drug acts. This might be a constant level in the blood or at the site of action of the drug or it might be a level varied from time to time by the operator according to the clinical need. In any case the variable infusion rate of drug is based on a prediction of what is going to occur in each individual patient based on what has occurred in previous studies.

The fact that the device delivers a drug at rates determined by (a) the program installed in the device, and (b) by data specific to a particular drug which is stored in the device, renders the infusion device, the calculation and the drug related data in combination a therapeutic device.

Such therapeutic devices are regulated by the laws of most countries and the efficacy and safety of all components of the device must be established in order for the device to be legally sold. The requirements to establish approval are extremely onerous and are often prohibitive to the commercial success of the device.

If one analyses a pre-programmed, target controlled therapeutic device it is apparent that it consists of two distinct parts:

- First, an underlying infusion system controlled by a microprocessor, similar in most ways to those currently marketed for fixed rate delivery of drugs, but able to change the delivery rate in response to an external control signal, and

- Second, a predictive control system which provides a signal to the first part to indicate to it the rate that drug must be delivered.

There are many devices consisting solely of the first part with no predictive element and these are generally less difficult to approve and are widely used for the delivery of drugs. As well, these devices have certain well established features to improve their functionality, but are in no way predictive, i.e. they perform simple stepwise calculations of multiplication or division of single values entered by the physician as well as functioning according to an internal timing system. Typical features are:

- An ability to alter characteristics of the device using a set up mode so that rate limits, drug units displayed on the screen, alarm signals, pressure limits, syringes to be used, dose rates to be used and communication settings may be altered. The changing of syringe size, for example, means that every change in rate is translated to movement of a mechanical part of the device after multiplication by a factor governed by syringe size.
- An availability, as a further refinement, to enter certain modes using a sequence of button presses not normally used by the user (IVAC Model 770).
- The availability of a communication connection to permit an external device to control the rate of delivery from the infusion device. Programs such as the Stanpump code running in desktop and laptop computers are able to provide control for a number of commercial infusion pumps such as the Grasseby 3400, the Ohmeda 9000 and the Harvard Apparatus Model 22 syringe pump.
- An ability to program a sequence of delivery rates indirectly by entering a set of volumes together with the time over which that volume must be given and then allowing the pump to form a process of division to calculate the actual delivery rate (IMED Gemini PC-1 or PC-2).
- The ability to enter an infusion rate, the body weight of the subject and the concentration of the drug to display the rate of delivery in a standardised form for easy interpretation (Grasseby 3400).

Each of these devices has features which extend the simple functions of entering an infusion rate such as mls per hour in order to deliver more complex

patterns. These features alter the way the device functions or displays information often by performing simple calculations but never predicting what will occur in the patient. Because of this they do not have to be evaluated in terms of their ability to achieve any prediction but merely as a device to control the rate fluid is delivered.

In contrast, infusion devices that incorporate a predictive element (Diprifusor-Zeneca) have required extensive clinical study to verify that the predictive model performs within certain defined limits in the patient population.

Summary of Invention and Object

The object of this invention is to provide a device which utilises a combination of features of prior art devices but has functional capability approaching that of the complex model based system by permitting the user to prescribe the delivery pattern to be used and to specify a simple multiplication process so that the overall size of the infusion pattern can be increased or decreased.

The invention therefore provides a system for controlling the operation of an infusion pump including means for controlling the rate of infusion of a drug or other solution by the infusion pump into a patient, user programmable microprocessor means for defining a predetermined rate of infusion profile or pattern for a predetermined drug or solution, a user operable scaling means for programming the microprocessor means to control the overall size of the predetermined rate infusion profile or pattern and thereby determine the amount of drug or solution delivered to the patient. and user operable means for activating the infusion pump to cause infusion of the drug or solution according to the user programmed information.

The system preferably includes user selectable means for selecting whether the scaling means is scaled according to body weight, body surface area or some other measure of the patient, such as estimated lean body mass.

The system may further include user programmable means for selecting a starting value for a scaling or multiplication factor for said scaling means.

In a preferred form of the invention, the system includes means for displaying in graphical form the predetermined rate of infusion profile or pattern as programmed by the user.

If desired, the system can include user operable means for entering into the microprocessor an identifying name for the programmed profile or pattern so that a particular profile can be selected from previously programmed information.

If desired, the system can allow for the use of a programming module having the necessary approval of a regulatory authority.

The key elements of a system embodying the invention are:

- the physician decides on the shape and magnitude of the delivery pattern
- the delivery rates used are at the discretion of the physician
- the administration is based on the prediction of the physician and not the device
- the device is evaluated on the basis of its ability to implement the prescription of the physician for the administration of the drug
- prior to administration and during administration, the device displays in graphical form the infusion rate pattern prescribed by the physician according to which the drug will be administered

To achieve the above features in the system, the physician or group of physicians is required, after purchase of the device, (i) to enter one or more sets of delivery rates and the times for which each rate is to operate; (ii) to name each of the sets of infusion rates so that a particular set may be chosen and the name of the set displayed during operation; (iii) to nominate whether this rate is to be scaled to the individual weight, body surface area or by some other measure of the patient; (iv) to enter a scaling factor or multiplication factor which will increase or decrease the overall size of the delivery rate pattern; (v) to nominate a starting value for this multiplication factor and also the range of values for the multiplication factor which he or she determines are suitable for that solution or drug, and (vi) to enter symbols or characters which identify the multiplication factor on the screen of the device.

By permitting the programming of the device in this way and scaling the overall magnitude of the delivery rate pattern according to the weight of the patient and by the multiplication factor, the physician is able to draw on his or her own knowledge and experience and to combine this with recommended safe rates of delivery of the substances to be infused. This knowledge is, of course, enhanced by published tables of delivery rates against the body weight of the patient and of delivery rates to achieve various clinical effects which are already available in the product literature describing the use of various pharmaceutical substances (e.g. product information of ICI-Zeneca Pharmaceuticals including recommended infusion rates of Propofol).

The importance of the system embodying the invention is that the simple scaling of the overall magnitude of an infusion pattern, determined by the physician and not by the supplier of the infusion device, permits practical administration of drugs without the need for complex computation and prediction in the device and hence avoids the need for any evaluation of the device in terms of therapeutic efficacy. This advantage has substantial commercial and practical importance.

Another advantage is that a modification of the pattern of the entered steps, of the multiplication factor or of the suggested ranges, can be made by the physician. This is particularly important if treatment groups with different requirements are identified, or if new information is obtained which would lead the physician to change his or her practice. In particular, it avoids the problem that predictions made by evaluators of therapeutic goods at one or more sites might not be referable to all sites.

The system embodying the invention can be further enhanced by the ability to use a programming module. Such a module might achieve a similar result to a physician but would permit a manufacturer of some new drug to recommend a delivery pattern on the basis of clinical trials. Such a module would become a therapeutic device separate and distinct from the infusion pump itself and would result in the manufacturer of the drug taking over the decision process of the individual physician. This of course would require evaluation and approval of the type employed for therapeutic substances.

Brief Description of the Drawings

In order that the invention may be more readily understood. one presently preferred embodiment of the invention will now be described with reference to the accompanying drawings in which:

Figure 1 is a flow chart showing the operational states of the system embodying the invention;

Figure 2 is an elevation of the front panel of the system illustrating a typical keypad and VDU showing a rate/time table running screen;

Figure 3 is a flow diagram showing the functional modes of the "Configure" mode of the operational states.

Description of Preferred Embodiment

The system embodying the invention is a medical infusion device or syringe pump designed primarily for the intravenous delivery of drugs associated with anaesthesia. It is microprocessor based with a keypad and LCD screen display. The system is mechanically and electrically similar to the systems described in our U.S. Patents 4,741,732 and 5,034,004, the contents of which are incorporated into the present specification by cross-reference.

The system has the facility to display the size, volume and concentration of drug in each syringe as it is loaded. As well. it is able to store the physical size of the subject being infused by the device.

Total body weight (TBW) of the subject may be entered to permit dosing according to units of body weight. The height and sex of the subject may additionally be entered to permit estimation of the lean body mass (LBM) or body surface area (BSA) for scaling dosing rate according to these parameters. Display of delivery rates can be in terms of millilitres of solution per hour or in terms of microgram of drug per minute per kilogram of TBW, LBM or BSA according to the mode of operation and the preference of the user.

The system has facilities to display alphanumeric and graphical information so that the operator can monitor operation of the device. Displays include general information to help with calibration of syringes. user programming and operation of the various modes of the device through to graphical display of variable infusion

rate patterns that have been programmed by the user. These graphical displays are presented prior to and during drug delivery.

The system embodying the invention is capable of automatic calibration to any plastic disposable or pre-filled syringe, before or during operation. It has electronic sensing of failure to deliver a drug due to incorrect engagement of the syringe. It can sense occlusion with an inbuilt force transducer calibrated to the syringe size. It also senses correct engagement of the drive head with a sensing device in the drive head. This contact sensor guards against accumulation of erroneous drug infusion data if the head is not engaged correctly and detects runaway where a syphoning effect causes the syringe to deliver a drug when the head is not driving it. During operation it displays patient and drug data and constantly updates delivery data assisted by a graphical display of the history and the anticipated events in the process. It has a delivery speed (flow rate) of 0.1 to 1400 ml/hr (dependant on syringe size) which is adequate for keep open rates through to bolus delivery. The drive is capable of delivering a force of up to 100 N but the maximum pressure which is set by the operator, is adjusted for syringe size using drive head force sensing. The pump has a linear infusion rate and linear drive positioning accuracy of plus or minus two percent.

The display is a 128 by 128 pixel back-lit LCD with a bit-map graphic capability.

The system embodying the invention is powered by 110/240V AC at 50/60 Hz or via four internal 1.2 amp hour lead acid gel batteries at 8V direct current providing 3 hours of battery operated use.

The system syringe pump has an extensive self-test and alarm system.

The system pump is equipped with operational modes for constant rate delivery, for keep open, for variable rate delivery according to a set of rate/time pairs entered by the user, for control of delivery rates by an external computer and for implementation of user supplied programs for executing special functions.

The ability to load tables of rate vs. time permits the user to enter data for producing variable rate infusions. This gives the user the opportunity to implement dosing regimens such as bolus and fixed rate infusions of antiarrhythmic, antibiotic

or chemotherapeutic drugs as well as more complex patterns suitable for establishing and maintaining constant arterial blood concentrations of anaesthetic agents.

An important feature of the use of tabulated rate/time information is the ability to scale the infusion rate, not only to the physical size of the patient but to scale the infusion rate with an arbitrary multiplication factor. With this capability the magnitude of the stored rate time table can be set, initially to the Plasma Drug Efflux values for a particular drug. This infusion rate is the rate on average to produce a blood concentration of 1 microgramme per millilitre of arterial blood in the patient. Then the value of the multiplier will be numerically equal to the predicted target concentration of the drug.

As well as entry of variable rate/time data tables directly from the keyboard, the system embodying the invention supports the use of Proprietary Modules which connect to the system communications port. Proprietary Modules perform an identical function to the user entering sets of named rate/time pairs and associated information from the keyboard. In general, Proprietary Modules are intended to permit the control of the rate of delivery of specific anaesthetic drugs such as thiopentone, methohexitone, propofol, fentanyl, alfentanil, remifentanil, midazolam, ketamine, atracurium, vecuronium, rocuronium and cis-atracurium according to infusion rates where recommendations have been made by pharmaceutical companies. A distinction of the use of Proprietary Modules over manual keyboard entry of infusion patterns is the ability to protect data for specific patterns from tampering.

To further enhance the ability to program variable rate patterns, the system is able to download stored tables to another similar unit, and to upload information from either another similar unit or a computer running software designed for manipulation of system information.

An additional major feature of the system pump is the provision for uploading control programs which can be supplied as a separate product and used at the discretion of the user. Uploadable programs are written to take control of the system embodying the invention according to interchange protocols. The basic aim

of such uploadable modules is to provide a shell around the system and generate infusion rates according to a new set of rules. Secondary to this role, uploadable programs can take over control of the VDU of the system to provide operational information.

Typical applications for this mode are:

- Patient control of the administration of drugs for pain relief or for sedation according to preset rules determined by a physician using a patient push button input,
- Feedback control of a physiological variables such as arterial blood pressure or a brain potential by sensing an electrical signal from a patient monitoring device using an analog input, and
- Control of an infusion with a predictive algorithm using an operator entered target arterial or effect site concentration and together with a predictive model of the drug levels in simulated compartments. Such models, which lack rigorous evaluation at present, are generally based on clinical studies of individual drugs. Models which might be implemented are the Compartmental Pharmacokinetic Model (CPM), the Plasma Drug Efflux (PDE) model with concentration dependant infusion rate profiles, as described in our U.S. Patent No 4,741,732, or some other, yet to be determined, model. In particular, the STANPUMP implementation of the CPM, which has achieved considerable popularity in the United States of America, can be supported by the system embodying the invention when written as an appropriate functional module.

The system embodying the invention can log operational data to a printer during normal operation. Data loaded from a Proprietary Module may be transferred to another similar pump in the teach mode.

Operational States of the System

The system provides seven main operational states. These operational functions, associated modes and logical pathways are shown in Figure 1 of the drawings and are described further below.

1. Power on Selftest

Power on Selftest checks for normal function of the device.

2. Configure

Configure permits altering functional characteristics of the device, loading variable rate infusion data either manually, with a proprietary module, from a PC or from another similar syringe pump which has been placed in the Configure state. Configure may also be used to load user supplied programs for special control functions from a PC.

3. Operational Modes

Operational Modes is the normal functional state of the system embodying the invention. Operational Modes has five separate modes, Fixed Rate Operate mode, Keep Open mode, Variable Rate/Time Table Operate mode, External Rate Control Operate mode and User Program Operate mode.

In the Fixed Rate Operate mode the pump delivers the drug at a constant rate set by the operator.

The Keep Open mode provides a delivery rate of 1.0 ml per hour (user alterable).

The Variable Rate/Time Table Operate mode provides delivery of the drug at variable rates against time according to a series of tables of data which have been entered by the user while in Configure. Each table, which must be named for identification and for generation of a menu, will contain a set of drug infusion rates against periods of time, to a resolution of 0.16 min, that each corresponding delivery rate is to occur for before moving to the next delivery rate. Infusion delivery rates are expressed in units of microgramme of drug per minute per kilogram of TBW, LBM or BSA of the patient. The rate/time pattern which has been read from the table of values may be increased or decreased in a proportional way by a multiplication factor which is stored with the rate/time table.

The multiplication factor may be altered by the operator from the keyboard. The purpose of the multiplication factor is to permit the operator to adjust the overall magnitude of the preset pattern of infusion while maintaining its shape. In association with each set of infusion patterns there are other items of information. Text may be entered to provide information about the pattern that is stored and this may be viewed with Assist. Text to appear to the right of the multiplication factor

in the display may also be defined to help operation. A default or starting value for the multiplication or scaling factor and a range of values for it may also be nominated. The purpose of this is to provide subsequent operators with convenient, on screen information about data that is stored in the device. When a named set of rate/time data is supplied by a Proprietary Module as opposed to data entered by hand or downloaded from a PC, the set of data is locked from modification. Data loaded from a Proprietary Module may only be removed or modified by attaching a Proprietary Module uniquely coded to match that set of rate/time data. Multiple sets of rate/time data may be loaded in any combination either manually, by download from a PC or from a Proprietary Module and are identified from a menu names for the data sets. To assist the operator, variable rate infusion patterns, once selected from the menu, may be previewed in graphical form prior to use as well as during operation. Rate/time information may be transferred from one system pump to another similar system pump irrespective of its original source, however, data originally loaded from a Proprietary Module may not be altered without attachment of a corresponding Proprietary Module. The downloading process may be used to clear all existing rate/time tables including those from Proprietary Modules. The Variable Rate/Time Table Operate mode accesses Syringe Identification and Calibration whenever the clamp lever is moved. This provides the operator with the ability to change syringes and to enter the concentration of drug in the syringe. When accessing Syringe Identification and Calibration from a particular variable rate/time table Syringe Identification and Calibration provides a default syringe drug concentration which has been specified in the variable rate/time table. The Variable Rate/Time Table Operate mode provides the elapsed time, the rate of delivery of the drug in units of microgramme of drug per minute and the accumulated dosage. Patient Data Entry is accessed from the Variable Rate/Time Table Operate mode to provide TBW, LBM or BSA of the subject depending on the units of drug delivery specified in the variable rate/time table which has been selected.

The Remote Control Operate mode permits delivery of a drug according to rates transmitted from an external control device.

The Upload Program Operate mode permits implementation of one or more special function program modules may be downloaded from a PC.

4. Syringe Identification and Calibration

Syringe Identification and Calibration is accessed from all Operational Modes and permits calibration of a new syringe, identification of a previously learned syringe and confirmation of the measured volume and drug concentration in a syringe.

5. Patient Data Entry

Patient Data Entry is accessed from the Fixed Rate Operate mode and the Variable Rate/Time Table mode and permits entry of patient total body weight (TBW) for scaling of infusion rates to patient size and entry of patient sex and height for the computation of patient lean body mass (LBM) and body surface area (BSA).

6. Assist

Assist may be accessed from all operational states except Power on Self Test. Assist provides the operator with information to help the operator to understand the various facilities in each operational state.

7. Bolus

Bolus is accessed from the Fixed Rate Operate mode, the Keep Open Operate mode and the Variable Rate/Time Table Operate mode to permit the operator to administer additional dosage.

User Interface

The user interface takes the form of the operator keypad, the VDU, the syringe clamp and the drive head. The preferred keypad and VDU are shown in Figure 2 of the drawings.

Operational Functions and Facilities

Referring again to Figure 1:

1. Power on Self Test

The preferred startup screen includes the text: System Test in Progress. Press "Assist" in all modes for operational information.

2. "Configure"

"Configure" permits altering functional characteristics of the device and the loading of variable rate infusion data by manual operation, by download from a PC, download from another similar system pump or by transfer from a Proprietary Module. Configure permits uploading of user programs. If CLR is held down at the end of Self Test, then Configure is entered. Configure has standard and advanced modes. The advanced mode of Configure is protected by password which may be unlocked by a jumper on the main system board. Figure 3 shows the functional modes of Configure.

When Configure is entered the Configure menu is displayed with the options - Setup, Advanced mode (password) and EXIT.

2.1 Setup

This mode permits review and editing of operator alterable settings in the system. The remaining alterable settings may changed in Advanced Configuration. The operator alterable settings includes: Bolus Rate; Occ. pressure; Runaway delay; Flow units; Alarm tone; Alarm vol; Time; K/O rate.

2.2 Advanced Configuration

The Advanced Configuration mode is entered from the initial Configure screen after entry of a valid password or after power on with the password jumper removed on the main board. This mode permits configuration of the system to perform a wide range of additional functions ranging from a simple Rate/Time table to permit the system to deliver drug according to a preset pattern through to advanced programmed functions limited by hardware capability and the basic control system. The Advanced Configuration menu includes the displays: Advanced Setup; Teach; Learn; Programme.

2.2.1 Advanced Setup

The Advanced Setup screen includes the displays: Keep open enabled; Time scale; Syringe identifn.

2.2.2 Teach

When the system embodying the invention is placed in the Teach mode it transmits all configuration and program data to another similar system pump which

is in the Learn mode. It requires use of the accessory interface cable and matching versions of Teach and Learn software modules to be installed in the system pumps. A sign-on and data packet transmission protocol is used to ensure the integrity of the transmission. The Teach Mode display includes: Teach Mode - V 1.0; Transfer all: •Settings •Rate/time tables •Program modules, from another CAiVAS in Learn mode, use cable (PN 0001).

2.2.3 Learn

When the system is placed in this mode it will receive and store configuration and program data in its entirety from another similar pump which is in the Teach mode. It requires use of the accessory interface cable and matching versions of Teach and Learn software modules installed in the system pumps.

A sign-on and data packet transmission protocol is used to ensure the integrity of the transmission. The Learn mode display includes: Learn Mode - V 1.0; Receive all: •Settings •Rate/time tables •Program modules, from another CAiVAS in Teach mode, use cable (PN 0001).

2.2.4 Program

On entry into the Program mode a menu of the various programming options is displayed as follows: Configure Programme Mode; Manual rate/time; Upload rate/time; Upload program.

2.2.4.1 Manual Entry of Variable Rate/Time Table

This mode supports entry of rate/time tables from the standard numeric keypad of the system pump. After entry into the Rate/Time Table mode a display of the names of the currently stored rate/time tables is presented plus the name "New Table".

If an existing table is selected, the Table Edit mode is entered and the data for that table displayed. Each table, which must be named for identification and for generation of a menu, will contain a set of drug infusion rates against periods of time, to a resolution of 0.16 min. that each corresponding delivery rate that is to occur for before moving to the next delivery rate. Infusion delivery rates are expressed in units of microgramme of drug per minute per kilogram of TBW or LBM of patient weight or square metre of BSA. The rate/time pattern read from

the table of values may be increased or decreased in a proportional way by a multiplication factor which is selected before operation. The multiplication factor may be altered during operation. The purpose of the multiplication factor is to permit the user to adjust the overall magnitude of the preset pattern of infusion while maintaining its shape. In association with each set of infusion patterns there are other items of information.

If "New Table" is selected a screen is displayed for naming the table. Numeric keys are used either for entry of both numeric or alpha characters. The Alpha Entry mode is entered by pressing ALARM. Entry of alpha characters is only available during the Manual Entry mode.

The Alpha Entry Mode is exited by pressing ALARM or by terminating entry of the character string by pressing ENTER twice. Correspondence between numeric keys and alpha characters is as follows:

1	ABC
2	DEF
3	GHI
4	JKL
5	MNO
6	PQR
7	STU
8	VWX
9	YZ-

Entry to the alpha mode is achieved by pressing ALARM once. These key equivalent codes are displayed in the lower half of the display during alpha data entry. The display of key equivalent codes is terminated by pressing ALARM a second time or on completion of entry of the character string. The three characters are displayed in the alpha mode by repeatedly pressing the corresponding key until the required character is displayed. When the desired character is displayed it is entered into the character string by pressing ENTER once. A second press of ENTER completes entry of the string. In the Manual Program mode once a character is displayed it is not necessary to hold down ALARM while cycling

through characters or displaying characters by pressing other numeric keys. After completion of entry of the name of the table, numeric values are entered by the supervisor successively down the column, each value is terminated by pressing ENTER. A rate/time pair is required on each line. The end of data entry in a particular column is signified by pressing ENTER a second time ie entering a NULL line. The rate/time data is headed by its name, identifying that table.

As well as entry of the name and a table of values other information may be entered to assist the operator. These are prompted and if entered are used instead of the default value during Operate Modes. Information which may be entered is (default):

Multiplication Factor (1.0)

High limit for multiplication factor (9999.9)

Low limit for multiplication factor (0.0)

Text to right of multiplication factor (~~bbbbbbb~~)

Patient scaling factor (LBM, BSA, TBW)

After entry, data may be reviewed and edited before exit from this mode. A review screen is displayed on selecting exit from the manual enter/edit screen. Data is presented as a simple graphic display in the units of milligram per minute per TBW, LBM or BSA to permit the operator to identify gross errors and confirm the shape of the infusion profile. Values are presented as a simple bar graph with time periods below and infusion rates scaled to the starting multiplication factor. The table edit screen may be re-entered by selecting EDIT or exited to the operate mode by selecting EXIT.

2.2.4.2 Upload Rate/Time Tables

Proprietary module upload.

This mode permits loading of rate/time table data using a Proprietary Module (PM). The module is attached to the system pump through RS232 plug and is powered by the data lines. This data supplied is identical to that supplied by manual entry of PC download but has in addition security codes to protect the data from alteration or copying once it is transferred to the system pump. Once a system pump is programmed by means of a PM the Teach, Learn and Programme

modes are inhibited until a PM with appropriate security codes is attached to the device. After programming of the device using a PM, a second PM can be attached to the system pump to update information in rate/time tables of the same name or adding programs with new names. When any PM is attached to the device, named sets of program information can be cleared from the memory of the system pump. Removal of all programs using the PM reactivates the Teach, Learn and Programme modes.

Computer Rate/time Table Upload

This mode permits downloading of rate/time table data from a computer into the memory of the system pump. It appends data to tables already present, if any. Data transmitted is identical to that entered in the Manual Entry of Variable Rate/Time Table.

Program Upload mode

This mode permits uploading program modules of any form compatible with the functional capability of the system pump. These modules must be written to interact with the system embodying the invention, but are able to interrupt the basic functions as an overlay of the core software. They may read all syringe calibration data, patient data and data available from A/D converter channels, the counter timer, the RS232 port and the data entry keypad of the system. They may take control of the VDU subject to interruption by the basic system for display of alarms. Examples of anticipated programme types are presented in the Appendix.

3. Operational modes

Referring again to Figure 1, the operational modes are entered directly from Power on Self Test. On entry this state a menu of the following operational modes is displayed according to the level of programming that has been installed by the supervisor. In the standard configuration, with no programming this menu is bypassed and the Fixed Rate Operate mode is entered directly. Once any of the available modes have been entered the only exit is a complete power off by lowering the syringe clamp without a syringe in place. This mode of exit provides for return to the previous operational state with reinstatement of variables using the

Last mode option. To implement this feature periodic backup to non-volatile store is required.

3.1 Fixed Rate Operate

The fixed rate mode is entered directly from Self Test using the Operational Mode selection screen.

3.2 Keep Open Operate mode

This mode provides a constant low flow rate irrespective of syringe size as set in the Setup Configure mode.

3.3 Variable Rate/Time Table Operate mode

On entering this mode the names of all available sets of Rate/Time Tables is displayed. Continuation screens are accessed by placing the cursor on "More" and pressing ENTER. When a name is selected, the system proceeds to the Rate/time table setup screen. This screen displays the name of the table followed by a multiplication sign, then the default value of the multiplication factor and the text to be placed to the right of the multiplication factor. It also displays the expected syringe concentration, the Patient size (TBW, LBM or BSA), the total dose given (0.0) and the elapsed time (00:00:00). The operator may proceed to edit any of the fields on the screen using ↑, ↓, numeric keys and ENTER.

The edited value of the multiplication factor is checked against the maximum and minimum values stored with the table. If the entered value of the multiplication factor is out of range, the system will warn the operator and will prompt for operator confirmation with operator warning message 2, "out of range". If the out of range value of the multiplier is accepted then the multiplier field will flash continuously during the infusion. When the cursor is moved to the Patient size entry the value, initially the characters TBW, LBM or BSA will be displayed, according to the characters stored with the table. When this field is accessed and ENTER pressed, the system enters Patient Data Entry (see section 5) for entry of TBW, as well as the sex and height if it is necessary to calculate LBM or BSA. On completion of Patient Data Entry the system returns to the previous mode and displays a Rate/time table setup screen. Once settings in the Rate/time table setup

screen are confirmed the Rate/time table run mode screen is entered by selecting EXIT.

The dose given and time can be edited so that if the power has been lost or if an infusion has already been started manually not using the system, then a known accumulated dose and elapsed infusion time can be entered so that the infusion begins from the appropriate time point in the infusion profile table. The assist menu for the Rate/time table setup screen displays the default infusion multiplier, the text to be displayed with it, the maximum and minimum values set for the multiplier, and the syringe concentration to be expected to be used with that Rate time table.

On starting the infusion the system displays a Rate/time table running screen. The system aligns the current position of the plunger drive with the stepper motor drive position. While running the system continually checks the stepper motor drive position against the plunger position. A record of dose given, flow rate and time elapsed is printed every thirty seconds. The system steps through the program infusion table based on the elapsed time and checks each rate read from the table against the maximum infusion rate limit. If the rate is greater than maximum then the pump is stopped and critical alarm number 3 is enabled and the infusion stops. Whilst running the infusion, if the syringe clamp is raised, the system returns to the Load Syringe screen. The system constantly monitors for the syringe being near empty and continually tests the battery condition. Whilst running, editing of the arterial concentration field is available with the normal checks on the entered value. The display of dose given, flow rate and time elapsed is also continually updated. Bolus and manual bolus are available during the program infusion running mode.

3.4 External Rate Control Operate

This mode permits control of the system pump with an external computer.

3.5 Program Operate

Individual Custom Programs are selected from the main Operate Modes menu. The nature of the display which appears once a custom program is entered is governed by the program. Rules for interface of programs with the system and

for VDU display are presented in Communications download and upload functions (see below).

4. Syringe Identification and Calibration

After completion of Power on Self Test or Configure, whenever the syringe clamp is raised, Syringe Identification And Calibration is entered and the system displays the Load Syringe menu.

5. Patient Data Entry

Patient Data Entry is accessed from the Fixed Rate Operate and Variable Rate/Time Table Operate modes and optionally from the Upload Programme Operate mode. In this mode the form of data entry is governed by the mode that has accessed Patient Data Entry. If access has been from Fixed Rate Operate, the operator is requested to enter the Total Body Weight (TBW) of the patient followed by the sex and the height in either inches or centimetres, if only the TBW is entered the prompt moves to the LBM prompt where a value may me entered. If height and sex have been entered a TBW and BSA are computed and displayed.

The cursor is then set on the sex field where ENTER is used to accept male and CLR is used to toggle to female. The weight is entered in kilograms with one decimal point. If the weight is set to zero then the lean body mass (LBM) field is entered manually. If the weight is not equal to zero then LBM is calculated. Height is entered in inches or centimetres. Height and weight may both be zero. Upon acceptance of the last patient parameter the LBM is calculated if height and weight is not zero. If either field is zero then LBM is entered manually. On first entry into this screen the system prompts for height in both centimetres and inches, however, once one unit is used, this unit is used alone for all further prompts for this field. Once the LBM has been calculated and printed on screen, the cursor moves to the LBM field and the LBM is available for editing. The cursor remains on this field until LBM is greater than 20.0 and LBM is less than 100.0. Once the LBM has been accepted the system returns to Fixed Rate Operate. BOLUS and START STOP cannot be used while editing the patient parameters.

If Patient Data Entry has been accessed from Variable Rate/Time Table Operate then the calculation will depend on whether the rate/time table which has been selected uses TBW, LBM of BSA and the basis for the variable rate infusion.

6. Assist

The Assist mode is accessed by pressing the Assist key at any time than in self test. Pressing any key returns to the screen from which Assist was entered.

7. Bolus

The bolus mode is available when the system is in the Fixed Rate Operate mode or Variable Rate/Time Table Operate mode. There are two methods by which drug may be delivered as a bolus. These are via keypad operation, or by manual push of the drive head. When a bolus is delivered by either means, the volume administered is measured and added to the VOLUME and DOSE displays of the Operate mode that has accessed Bolus. The delivery of a bolus does not affect the computation of a rate/time table, that is to say that bolus delivery proceeds simultaneously with the computation of drug delivery according to the rate/time table.

Keypad bolus

By pressing and holding down BOLUS on the keypad, drug is administered.

Manual bolus

By releasing the drive head drug may be delivered by hand at a rate determined by the operator.

Alarm condition sensing and display

Alarm conditions are sensed continuously during all operations in the system. Alarm conditions are categorised into two types. These types are critical and non-critical.

Non Critical Alarms

The non-critical alarm conditions are:

- Occlusion force check failed
- Head disengaged during an infusion (> 20 s, indicates syringe runaway)

- Syringe clamp opened during an infusion
- Syringe Near empty (< 5 min of drug or < 10 mm of plunger travel)
- Syringe empty

Critical alarms

The critical alarm conditions are:

- RAM check fail
- EPROM check fail
- Stack checking failed
- CPU watchdog check failed
- Battery check failed (< 80% of full voltage)
- Head position - stepper position discrepancy

Communications download and upload functions

RAM operations, EPROM and EEPROM

On startup, stored data from EPROM and EEPROM is loaded into RAM. The EPROM contains system code, drug programme data and programmed system parameters. The EEPROM is battery backed up storage which can be dynamically programmed. It holds a table of the last four syringe sizes calibrated on the system in a table.

When a syringe is loaded, the system checks to see if its size matches one in the table. If so it uses the corresponding calibration. If not the system would proceed to the syringe calibration menus.

Runtime checking operations

The system embodying the invention performs the following runtime checks when not running an infusion:

- Clamp raised
- RAM check
- Stack check
- Battery check

The system performs the following runtime checks when running an infusion:

- Clamp raised

- RAM check
- Stack check
- Battery check
- Update infusion rate onscreen

User Loadable Programs

The system is capable of a number of further options for user loadable programs which would be suitable for executing in the system environment. They represent a wide range of medical applications where the final path is the delivery of a biologically active substance according to a set of rules either of a predictive nature, in response to some external signal or a combination of the two. Examples of suitable programs are described below.

Alarm System Based on Physiological Signal

During execution of the Fixed Rate Operate or Variable Rate Operate modes an additional program will permit sampling and analysis of an analogue signal describing some respiratory or cardiovascular function and the generation of an alarm and infusion "shut off" if preset limits are exceeded.

Patient Controlled Administration

Programs for implementation of Patient Controlled Analgesia (PCA) are readily implemented in the system. Such techniques are currently implemented in infusion pumps manufactured by Grasseby, Abbott and others. These devices permit the physician to enter a set of parameters for infusing an opioid analgesic, particularly morphine, pethidine or fentanyl via the intravenous route or administration of lignocaine or bupivicaine via the epidural route. Delivery in this mode is usually a series of pulses of drug administration where the rate and duration of the pulse is defined. As well, a background maintenance rate may be selected. Pulses of drug are usually triggered by the patient pressing a momentary closure-push button switch connected to the digital input of the system. The operator can set the number of pulses which are acknowledged in a set period eg. one hour. The software has the ability to store the usage pattern of the patient for up to some days. The usage pattern of the patient may be reviewed by scrolling on the VDU or by printing via the RS232 port. A particular requirement, when

restricted drugs are used is the provision of physical locking to prevent access to the syringe or connectors once one has been loaded. This would be best implemented with a special purpose mounting bracket which incorporates a plexiglass lockable cabinet to enclose the system. Details of this locking may be obtained from existing devices.

Delivery Based on Feedback from a Biological Signal

A second form of program is one that implements a control algorithm to maintain a physiological variable within certain limits according to an electrical signal indicating the magnitude of a physiological variable. A widely used example of this is the control of arterial blood pressure by infusion of drugs that increase or decrease the resistance of the circulatory system or alter the function of the heart. A further application, which does not have wide application at present, is to sense breathing patterns during delivery of drugs which might impair breathing. Delivery of an anaesthetic agent might also be adjusted according to a signal derived from the spontaneous electrocardiogram of from an evoked response.

Predictive Model of Patient Drug Concentration

A further type of programme is to control delivery of a drug, most particularly an anaesthetic agent, according to predictions from measurements in previous subjects.

Plasma Drug Efflux

An extension of the Rate/Time Table Operate mode is implementation of the Plasma Drug Efflux (PDE) function where infusion rates generated according to predictions of the rates required to maintain a constant arterial blood concentration of an infused drug in the arterial blood. Infusion rate data are entered in the form of tables of values of infusion rate against the period the rate is to run. A table may contain single set of infusion rates or multiple infusion rate profiles where each is associated with a specified target arterial blood concentration. The first column of each table specifies a series of periods of time, to a resolution of 0.16 min, that each corresponding delivery rate is to run for before moving to the next delivery rate. Subsequent columns, up to ten in number, contain a set of infusion rates, normalised to 1.0 ug/ml of target concentration and 1.0 kg of lean

body mass (LBM), corresponding to each time period. Each column is headed by a specific target concentration (ug/ml) to identify the infusion rate profile contained in that column. Each column may have twenty values. Successive columns are entered with headers of target concentrations in ascending order from left to right. Subsidiary tables may be stored under the name of a primary table when a factor exists which is known to alter the overall relationship between the infusion rate and time, eg the addition of nitrous oxide or a profile specific to children. During operation in this mode similar calculations are performed as in the standard Variable Rate/Time Table Operate mode, however, in a Upload Programme Operate mode the multiplication factor is replaced by a Target Blood Concentration (C_T) which is expressed in units of microgrammes of drug per millilitre of patient arterial blood and the tabulated values are expressed in terms of units of Plasma Drug Efflux (millilitres of blood cleared of drug per minute per kilogramme of subject TBW or LBM). The major feature of the PDE function is the ability modify the infusion rate according to predicted changes in the PDE according to the C_T. An example of a PDE table is shown below:

PDE Table Layout

Target conc-mcg/ml Time-min	10.0 Rate ml/min/kg	15.0 Rate ml/min/kg	20.0 Rate ml/min/kg
0.0	10.0	15.0	20.0
1.0	5.0	10.0	15.0
2.0	4.0	5.0	10.0
4.0	3.0	4.0	5.0
8.0	2.5	3.0	4.0
16.0	2.0	2.5	3.0
32.0	1.5	2.0	2.5
64.0	1.0	1.5	2.0

Compartmental Pharmacokinetic Model

Another form of prediction is the Compartmental Pharmacokinetic Model (CPM) function which utilises microconstants for a one, two or three compartment

pharmacokinetic model, stored in the device, to predict an infusion rate pattern suitable for establishing and maintaining the C_T irrespective of how it is manipulated by the operator. Microconstants for a one, two or three compartment pharmacokinetic model may be stored. Sets of microconstants are identified by a name usually referring to the relevant drug eg. V1 (ml/kgLBM) and k10 (per min) for a one compartment model, V_1, k_{10}, k_{12} and k_{21} for a two compartment model or V_1, k_{10}, k_{12}, k_{21}, k_{13} and k_{31} for a three compartment model.

Sets of microconstants would generally be identified by a name eg. PROGRAMME 1, PROPOFOL or ATRACURIUM. The number of compartments would be stored following the name. This is followed by constants describing the model.

Complex Predictive Model

The PDE approach is valid for establishing and maintaining a range of arterial blood concentrations provided that rate/time tables are used which cover the values of C_T used. The method used to derive PDE does not incorporate methods for predicting infusion requirements to make step changes from one value of C_T to another once the infusion is under way.

The CPM is widely used to predict dosing requirements for making step changes in C_T. The CPM, derived from drug elimination profiles, does not allow for concentration dependent changes in the model and is unlikely to be sophisticated enough to accurately model sudden changes in C_T. New approaches to modelling, using deconvolution or neural networks to derive more sophisticated simulations are likely to emerge in the future. The system embodying the invention provides an adequate operator interface as well as computational capability to permit implementation of these methods as they become available, with minimal delay due to the design process.

CLAIMS:

1. A system for controlling the operation of an infusion pump including means for controlling the rate of infusion of a drug or other solution by the infusion pump into a patient, user programmable microprocessor means for defining a predetermined rate of infusion profile or pattern for a predetermined drug or solution, a user operable scaling means for programming the microprocessor means to control the overall size of the predetermined rate infusion profile or pattern and thereby determine the amount of drug or solution delivered to the patient, and user operable means for activating the infusion pump to cause infusion of the drug or solution according to the user programmed information.

2. The system of claim 1 further including user selectable means for selecting whether the scaling means is scaled according to body weight, body surface area or some other measure of the patient, such as lean body mass.

3. The system of claim 1 or 2, further including user programmable means for selecting a starting value for a scaling or multiplication factor for said scaling means.

4. The system of claim 1, 2 or 3, further including means for displaying in graphical form the predetermined rate of infusion profile or pattern as programmed by the user.

5. The system of any preceding claim, further including user operable means for entering into the microprocessor an identifying name for the programmed profile or pattern so that a particular profile can be selected from previously programmed information.

6. The system of any preceding claim, wherein the user programmable microprocessor means is programmable (i) to enter one or more sets of delivery rates and the times for which each rate is to operate; (ii) to name each of the sets of infusion rates so that a particular set may be chosen and the name of the set displayed during operation; (iii) to nominate whether this rate is to be scaled to the individual weight, body surface area or by some other measure of the patient; (iv) to enter a scaling factor or multiplication factor which will increase or decrease the overall size of the delivery rate pattern; (v) to nominate a starting value for this

multiplication factor and also the range of values for the multiplication factor which he or she determines are suitable for that solution or drug, and (vi) to enter symbols or characters which identify the multiplication factor on the screen of the device.

7. The system of any preceding claim, further including a programming module containing an infusion pattern based on clinical trials or other data.

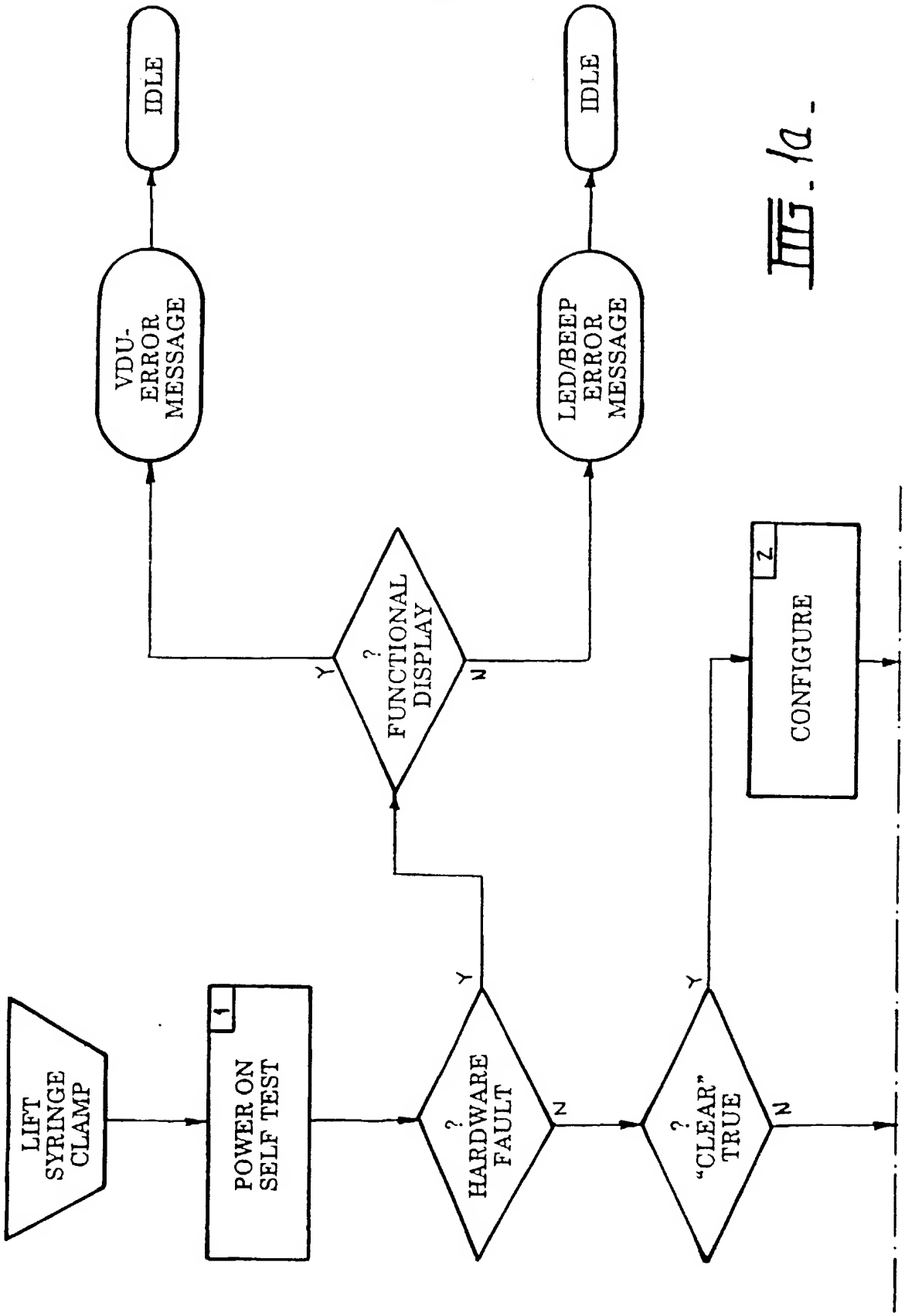

LIFT SYRINGE CLAMP
POWER ON SELF TEST
1
? HARDWARE FAULT
Y
N
? "CLEAR" TRUE
Y
N
CONFIGURE
2
? FUNCTIONAL DISPLAY
Y
N
VDU-ERROR MESSAGE
LED/BEEP ERROR MESSAGE
IDLE
IDLE

FIG. 1a.

FIG. 1b.

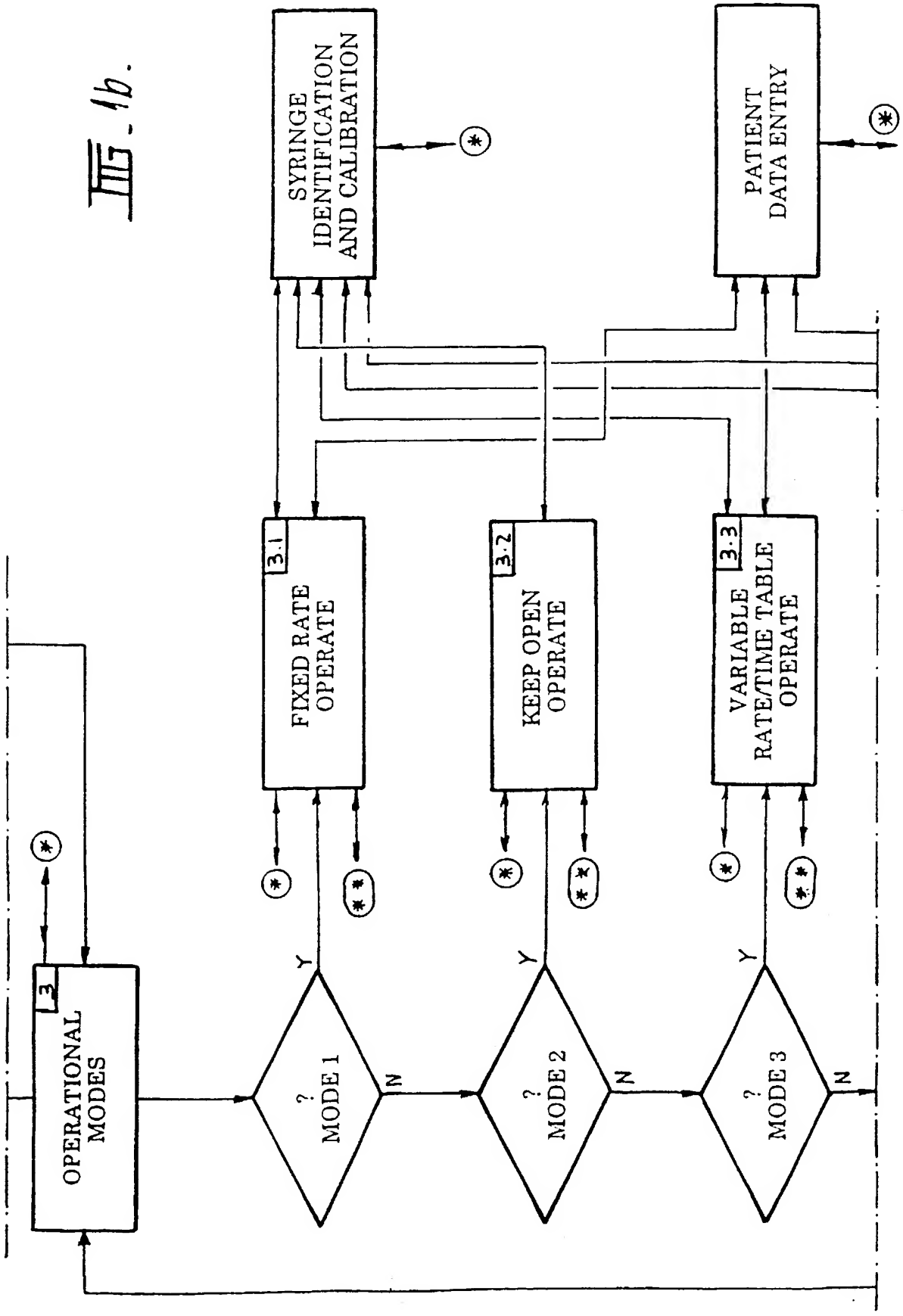
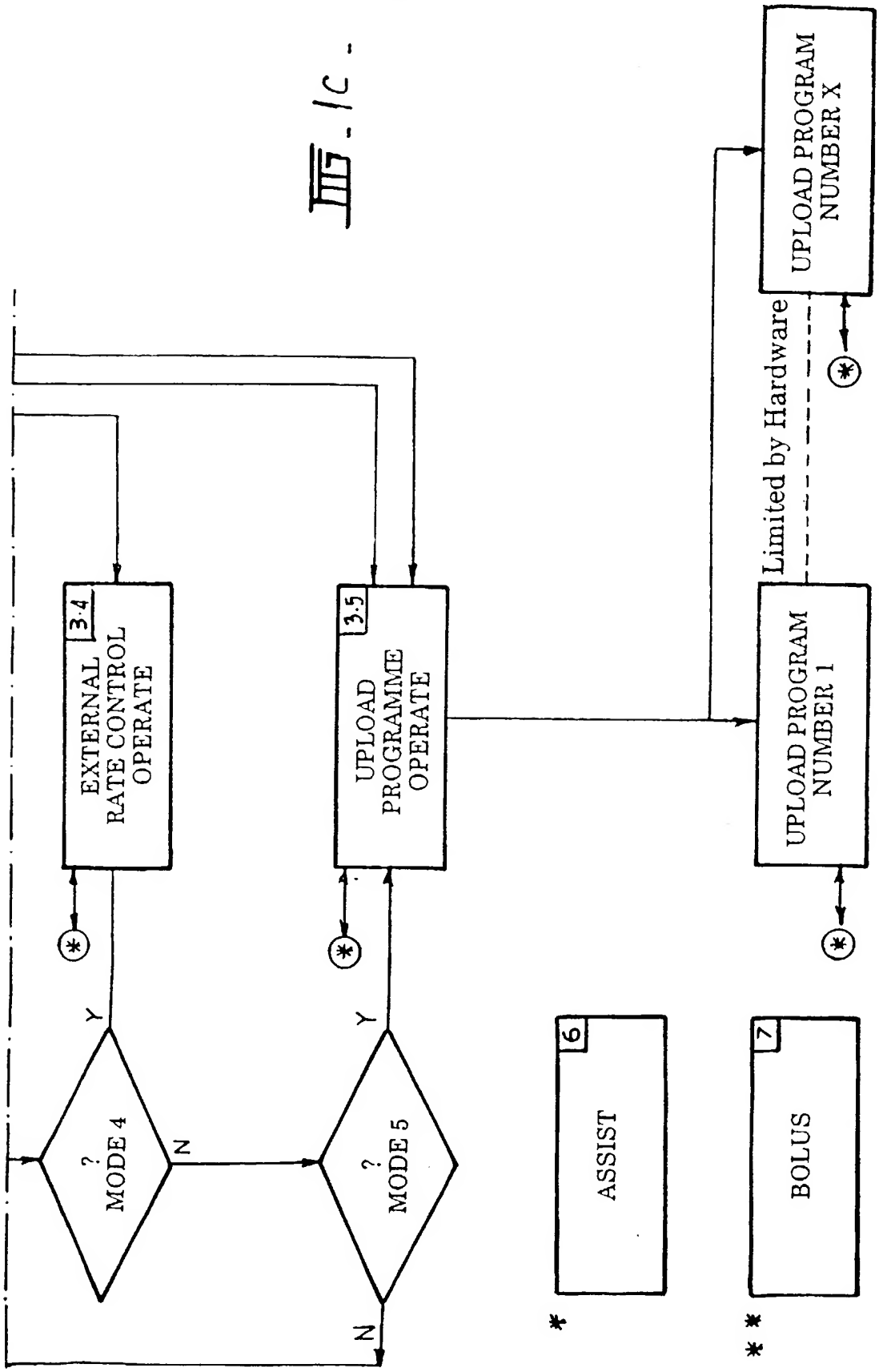

SYRINGE IDENTIFICATION AND CALIBRATION
PATIENT DATA ENTRY
3
OPERATIONAL MODES
3.1
FIXED RATE OPERATE
3.2
KEEP OPEN OPERATE
3.3
VARIABLE RATE/TIME TABLE OPERATE
? MODE 1
? MODE 2
? MODE 3
Y
N
*
**

FIG. 1C


UPLOAD PROGRAM NUMBER X
Limited by Hardware
UPLOAD PROGRAM NUMBER 1
3.4
EXTERNAL RATE CONTROL OPERATE
3.5
UPLOAD PROGRAMME OPERATE
Y
? MODE 4
N
Y
? MODE 5
N
6
ASSIST
7
BOLUS

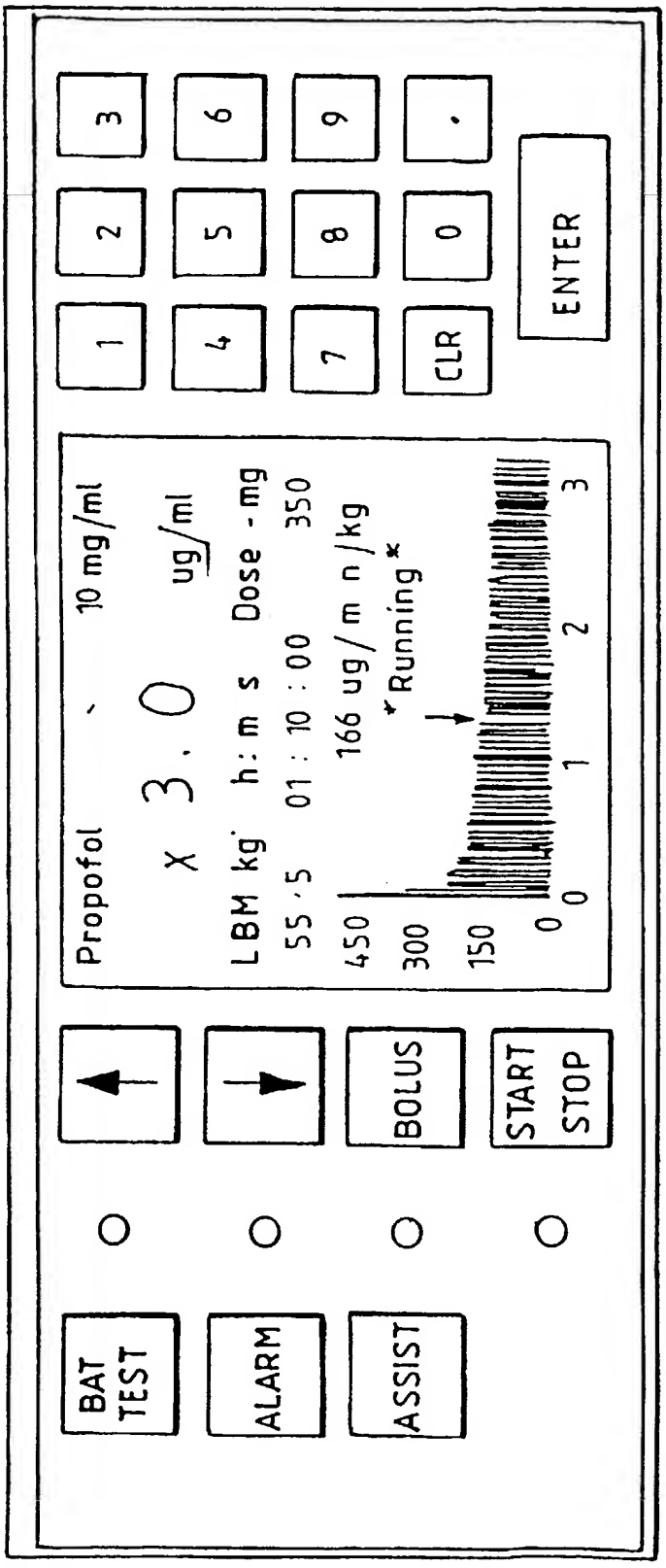

BAT TEST
ALARM
ASSIST
BOLUS
START STOP
Propofol 10 mg/ml
X 3.0 ug/ml
LBM kg h:m s Dose - mg
55.5 01:10:00 350
166 ug/m n/kg
Running
450
300
150
0
0 1 2 3
1 2 3
4 5 6
7 8 9
CLR 0 .
ENTER

FIG. 2.

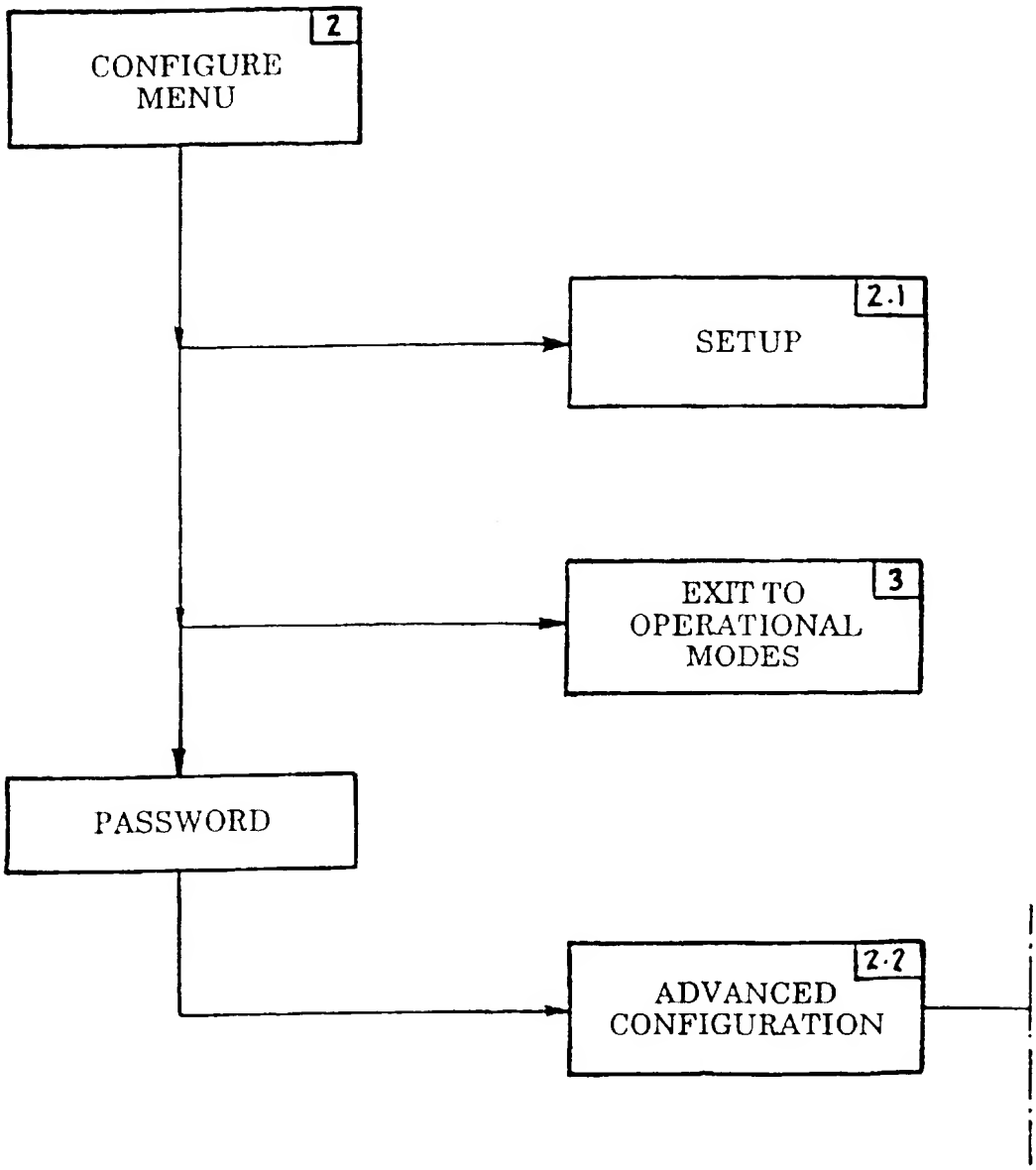

2
CONFIGURE MENU
2.1
SETUP
3
EXIT TO OPERATIONAL MODES
PASSWORD
2.2
ADVANCED CONFIGURATION

FIG. 3a.

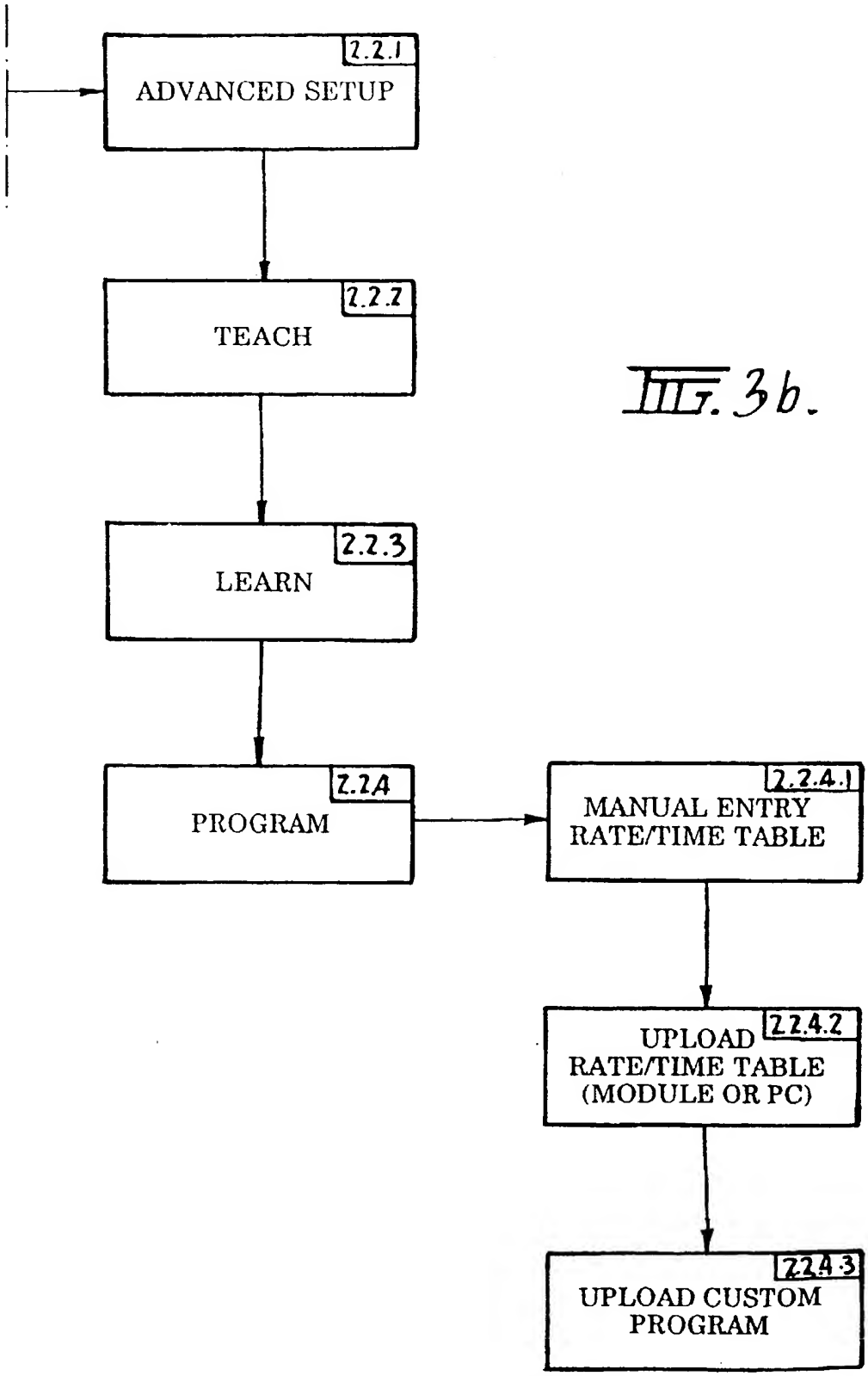

2.2.1
ADVANCED SETUP
2.2.2
TEACH
2.2.3
LEARN
2.2.4
PROGRAM
2.2.4.1
MANUAL ENTRY
RATE/TIME TABLE
2.2.4.2
UPLOAD
RATE/TIME TABLE
(MODULE OR PC)
2.2.4.3
UPLOAD CUSTOM
PROGRAM

FIG. 3b.

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/AU 96/00801

A. CLASSIFICATION OF SUBJECT MATTER

Int Cl[6]: A61M 5/142

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC : A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
AU : A61M 5/142, 5/14, 5/00

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
DERWENT : (A61M-5 or F04B - 43 or G05B - 19) and (control: or program: or automat:) and (profil: or pattern:) and (infus: or intra( )ven:) and (scal: or sizing or size#)
JAPIO : same as Derwent

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
	EP 702966 A (MEDRAD, INC.) 27 March 1996	
X	summary of invention, page 4 line 42 - page 5 line 27, entire document	1-5, 7
Y	page 4 line 42 - page 5 line 27	1-3
	EP 364010 A (C.R. BARD, INC.) 18 April 1990	
X	column 2 line 51 - column 3 line 34, entire document	1-3
Y	column 2 line 55 - column 3 line 1	1-3
	WO 93/04713 A (THE UNIVERSITY OF MELBOURNE) 18 March 1993	
X	page 4 line 1 - page 6 line 25, entire document	1-3
Y	abstract lines 5-6	1-3

[X] Further documents are listed in the continuation of Box C

[X] See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 January 1997	29 JAN 1997

Name and mailing address of the ISA/AU	Authorized officer
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INTERNATIONAL SEARCH REPORT

International Application No.
PCT/AU 96/00801

C (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	EP 226268 A (BAXTER TRAVENOL LABORATORIES, INC.) 27 June 1987	
X	page 2 line 10 - page 3 line 15, figure. 1, page 4 lines 16-17	1, 4
Y	page 3 lines 1-11	1
	WO 94/07186 A (GRASEBY MEDICAL LIMITED) 31 March 1994	
X	entire document	1, 4
Y	page 1 lines 21-25	1
	WO 84/03218 A (THE JOHNS HOPKINS UNIVERSITY) 30 August 1984	
X	page 2 line 24 - page 3 line 25	1
Y	page 3 lines 20-25	1
	WO 93/25816 A (SABRATEK CORPORATION) 23 December 1993	
X	page 2 line 14 - page 3 line 25, figure 1, entire document	1
Y	page 2 lines 17-19	1
	WO 92/18175 A (NOVO NORDISK A/S) 29 October 1992	
Y	page 1 line 30 - page 3 line 5, entire document	1-4
	WO 94/12235 A (ABBOTT LABORATORIES) 9 June 1994	
Y	summary of the invention, entire document	1-4
	US 5389071 A (KAWAHARA et al) 14 February 1995	
Y	column 4 lines 3-61, abstract	1-3
	EP 544393 A (IMED CORPORATION) 2 June 1993	
Y	column 3 line 3 - column 5 line 6, entire document	1-3

INTERNATIONAL SEARCH REPORT
Information on patent family members

International Application No.
PCT/AU 96/00801

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member					
EP	702977						
EP	364010	AU	30946/89	CA	1327498	CN	1042659
		JP	2146281	NZ	228726	US	4943279
WO	9304713	AU	25870/92	EP	603304	US	5409456
EP	226268	CA	1274737	JP	62034571	US	4785799
WO	9407186	GB	9219875				
WO	8403218	US	4731051	CA	1207871	EP	137789
		GB	8424624	GB	2146460	IT	8323311
		IT	1219342	US	4373527	US	4525165
		US	4573994	US	4619653	US	4784645
WO	9325816	AU	30682/92	EP	655107	US	5395320
WO	9218175	AU	16823/92	DK	694/91	EP	580723
WO	9412235	AU	56063/94	CA	2150258	US	5378231
		US	5547470				
US	5389071	JP	5277181				
EP	544393	AU	29646/92	CA	2083666	US	5219330

END OF ANNEX